July 14, 1949.

Dr. H. B. Newcombe,
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Dear Howard:

Thanks for the data and MS. I am enclosing a postcard to tell whether you want the MS back- it wasn't clear from your letter. I couldn't help noticing that my name is misspelled Lederburg throughout (p.9, 11), just in case you are publishing it in this form.

Your segregation data certainly show rather more duplex prototrophs than I have noticed either as sectored colonies on EMS, or in phage tests. This needs some looking into. By details on your procedure. I meant such things as the composition of your complete and minimal media, and your washing fluid, if they deviate in any way from what I have in print.

The data in cross A certainly do not seem to be in accord with B as far as the numerical proportions go ( 20/86 against 1/67 ), but I have sometimes noticed such discrepancies in replicate crosses. With more data, the reversed cross segregations should approach the same ratios for the corresponding crossover classes. Even barring this inconsistency, I think it would be premature to rely on the position of sr to the "left" of BM on these data. sr should be tested against the $B_1$ segregation (most conveniently by using minimal with and without thiamine) and if it doesn't show tight linkage there, then also with Mal (as in W-677) the troubles with which I think I wrote you in my last letter. Since last writing, I've isolated a segregant which, like W-677, is $TLB_1$- Lac- Mal- etc., but in crosses with 58-161 gives almost all Lac and Mal , instead of the expected excess of - prototrophs. Lac and Mal still do not appear to be linked, and I am as far from understanding it all as ever, but the behavior of this segregant lends support to the idea of some very peculiar chromosomal shenanigans! If you should ever prepare a W-677sr stock, I would appreciate having it. My interest is mainly in having another genetic marker,

As to overlapping of work (which is not always bad) Demerec is the man to confer with, as I don't come into it at all. Mr. Zinder went to CSH to take the phage course, and is working as an assistant to Demerec partly to show them how to make crosses (!) and partly to broaden his own outlook a little with these new contacts. His research problem here is with Salmonella, but I thought we might try to test dominance of some drugresistance factors in the heterozygotes if we could.

From what I was able to gather at the Shelter Island Gene Conference last month, Demerec is pushing along lines very similar to your own, except for a greater emphasis on the shifts back and forth from dependence to sensitivity, which he seems to have carried out any number of times.

I would not be greatly surprised if many of the sensitive types obtained from sd by selection in the absence of streptomycin turned out to be suppressor mutations: viz., abstracts, pp. 617-618, Genetics 33, 1948.

Your radiation differences remind me of Giles' latest work on inositolless reversions in Neurospora. He has a number of alleles with different spontaneous reversion rates. His patterns agree with the notion that there may be alleles which can be reverted spontaneously (thermal energy), others which need the greater energy of a UV quantum, and still others which respond frequently only to the heavier kick of X-rays. I think it may be unfair to say that we know nothing of the differences between spontaneous and induced mutations— consider Stadler's investigations in maize for example!

I have really very much appreciated the opportunity of seeing your latest work, and thank you for it.

Sincerely yours,

Joshua Lederberg.